Get Real

Real-Life Data in Drug Development

GetReal - Project No. 115546

WP1: Deliverable D1.6 Early use of pragmatic designs in medicine development

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1. Executive Summary

This document describes the outcomes of stakeholder engagement undertaken by Work Package 1 of GetReal which had the aim of eliciting a comprehensive stakeholder view on the acceptability and usefulness of pragmatic clinical trials for establishing relative effectiveness of new drugs. Stakeholder opinions are based on discussions during a workshop that was held on 9 September 2015.

Workshop overview

This workshop combined presentations, group breakout sessions and plenary discussions with the aim of exploring the key challenges of incorporating early pragmatic trials into medicines development frameworks.

Workshop objective

To understand stakeholder views regarding pragmatic clinical trials, conducted prior to market authorisation, as sources of data on relative effectiveness that can be used in regulatory and/or reimbursement decision-making: study timing and design, the strength of evidence on effectiveness, acceptability for decision making and the generalisability of results.

Overall message/conclusions

The use of pragmatic clinical trials in medicine development is still very much in its infancy and most of the proposals put forward in this workshop are theoretical because practical experience from the perspective of all stakeholders in this field is very limited. Conclusions on the acceptability of pragmatic approaches in medicine development will develop with time as decision makers are given opportunities to gauge the acceptability of pragmatic elements of trial design in routine practice. In the meantime, initiatives which set out to understand the factors that contribute to the efficacy-effectiveness gap will be of increasing importance in order to identify where pragmatic study elements may have the greatest impact (for instance by further literature reviews of regulatory and health technology assessment (HTA) challenges, as undertaken in this case study). It is expected that this type of due diligence will identify elements on the pragmatic continuum that can be implemented early in a clinical development programmes to meet specific effectiveness challenges. Different challenges may require different levels of pragmatism and review of whole development programmes, rather than individual studies, will allow pharmaceutical R&D to consider what activities can be stopped or reduced if additional pragmatic clinical trials (PCTs) are planned. It will also allow consideration of the most efficient ways of

addressing effectiveness challenges within the programme, either by increasing pragmatism of traditional randomised controlled trials (RCTs) or including new PCTs.

Questions still remain regarding the situations in which pragmatic elements could add the most value to the clinical development process and when is the best time to incorporate them. Best practice guidelines on the use of early pragmatic designs/elements will help to allay these uncertainties in the design of future PCTs. Collaborative efforts such as case studies and evidence synthesis from disparate sources will also provide insight in this respect. Moreover, a greater use of the joint regulatory/HTA scientific advice process will help determine how pragmatic elements can be brought into traditional RCT in order to improve estimates of effectiveness and reduce uncertainty in decision making by stakeholders. It should also be borne in mind that the most conservative and most widely implemented RCT designs may not always be the most appropriate.

2. Stakeholder views on the usefulness and acceptability of pragmatic clinical trials

Stakeholder opinions are based on discussions during a workshop that was held on 9 September 2015. In order to encourage openness and sharing of information, the workshop was held under Chatham House rules which means that neither the identity nor the affiliation of the speakers, nor that of any other participant, is revealed. During two separate group breakout sessions, participants explored how early PCTs could address effectiveness challenges. The participants debated various aspects of PCTs and explored the acceptability and value of early PCTs to a range of stakeholders (payers, regulatory, patients, pharmaceutical R&D).

Breakout session 1:

Participants were divided into three groups to discuss the following two questions:

Question 1: Which effectiveness questions would pragmatic designs best address?

OBJECTIVE: Identify which effectiveness questions would be regarded by stakeholders as particularly suited to be addressed by early PCTs

Overall summary:

The majority of views indicated that PCTs had a clear role in situations when RCTs can't answer the question of effectiveness; in particular when **efficacy is not predicted to match effectiveness**, for reasons such as patient characteristics, comorbidities, real-world patient behaviour (for instance. adherence), expected differences between old and new drug profiles, or the way health systems provide their service. However there is clear need to understand when efficacy and effectiveness are going to be different to inform decisions on whether or not to implement PCTs.

It was suggested that PCTs could **allow enrolment of a greater number of patients** than traditional RCTs and therefore would allow expansions of populations of interest. Pragmatic designs were also viewed as beneficial for establishing **effectiveness in subgroups of the general population**, especially those which may otherwise be excluded from conventional RCTs due to more stringent inclusion/exclusion criteria. Moreover, there was a preference for the ***a priori* identification of subgroups** on which the study could be designed, rather than *post hoc* subgroup derivation and evaluation. However, it was pointed out that subgroup analyses in PCTs could be difficult to conduct, for instance in situations where there is variety of usual care.

PCTs could generate valuable evidence on **acceptability by patients** in real practice and for **confirming positioning** of new treatment in treatment paradigms.

There was a general consensus among stakeholders that a particular benefit of pragmatic designs is the ability to capture effectiveness of drugs when **comparators are used in a manner in the real world that can't be replicated in RCTs**, for instance when a medicine is used off label. Moreover, PCTs could be beneficial in situations where s **wide variability in usual** care makes it hard to define a single comparator arm, or when there is interest in comparing to a treatment guideline or strategy.

PCTs were generally thought of as **long-term trials** especially since they can be **more adaptive**, incorporating advances in clinical practice, the arrival of additional comparators, and accumulation of knowledge of the disease.

Group 1

Stakeholders in this group included representatives from the pharmaceutical R&D, health technology assessors and academia. Participants provided a range of views on when PCTs would be useful and conversely when they would not be expected to be useful.

Stakeholders indicated that the key value for PCTs was in disease areas or clinical settings where efficacy and effectiveness are thought to be very different. It is therefore important to be able to predict where this is the case early in the drug development. Particular value was seen for PCTs in diseases where there are multiple treatment options and a variety of clinical practice, which could not be assessed in a traditional RCT.

Perspectives of individual comments are noted after each comment: Pharma R&D (Pharma), health technology assessors (HTA), Analytical/Academic (Acad).

PCT useful	PCT (less or) not useful
If efficacy and effectiveness are thought/expected to be very different (Pharma/Acad)	If efficacy and effectiveness are thought to be very related
Multiple active comparators & other therapeutic options & a variety of clinical practice (Pharma/HTA)	In head-to-head comparisons. For example to compare treatment A to treatment B.
For combinations of treatments (Pharma)	Where indirect comparison can substitute PCT data (Pharma)
For incorporating endpoints that are not possible in RCT (Pharma)	In situations where there is limited scope for flexibility in practice or when patient population are not going to be diverse/broad (HTA)
In special populations (elderly, comorbidities) (Pharma)	If infrastructure to embed PCT in clinical practice is lacking (HTA)
In a more general population (but also with the aim of identifying which subgroup(s) has the greatest benefits) (Pharma/Acad)	If interpretation is difficulty due to heterogeneity: underpowered subgroups, need extreme numbers or follow-up trials in subsamples later (Pharma/Acad)
For incorporating/accommodating changing landscape and evolving understanding of disease and treatment effects. Compared with the more static protocol of RCTs (Pharma)	For vaccinations (Acad)

To unearth issues/knowledge of clinical practice earlier on (Pharma)	In situations where outcomes which require special testing or for procedures (Pharma)
For orphan indications (to increase the number of subjects) (Pharma)	When measurement of outcomes requires specific expertise.
If patients are very different in real life than in RCT, for instance with respect to adherence, long term treatment (Acad)	
For additional information on safety, as supplementary study (Acad/Pharma)	
To establish the level of influence of intervention on resource use – for cost-effectiveness analysis in HTA submissions (Acad/Pharma)	
Watch clinical practice	
Medical significance	
Long term data	
Study drop-out in induction phase (side-effect)	
To capture off-label use post-launch (Pharma)	
For utilising EHR and to actually observe what GPs are doing, observe actual dosing and corresponding treatment effect and adverse events (Pharma)	

* Stakeholder perspectives: Pharma R&D (Pharma), Health technology assessors (HTA), Analytical/Academic (Acad)

Group 2

Stakeholders in this group included patient representatives and representatives from the pharmaceutical R&D, regulatory (both pharma and public sector), and health technology assessors. In addition to the themes mentioned by group 1, the stakeholders indicated that PCTs could be useful for collecting more clinically relevant outcomes and provided opportunities for collecting more long-term outcomes than traditional RCTs would. The potential to better engage patients and other healthcare stakeholders was also emphasized.

When PCT is useful:

- Population
  - For targeted populations/subgroups (Reg)
  - Can include broader population than RCTs, more relaxed exclusion criteria
- Outcomes
  - Potential to collect more clinically relevant outcomes (Reg/HTA)
  - Patient reported outcomes (PROs). More real life PROs in PCTs could be aligned with guidelines (Pat)
- Assessing interventions embedded in a real-world setting
  - Some concern however on over-reliance on “real world” and “soft” PROs, which might give soft and messy data. Strictly guideline-driven trial could be an

alternative to embedding in imperfect (non guideline-compliant) clinical practice since patients often might prefer clearer disease management (Pat)
- Opportunities for broader stakeholder engagement than RCTs (Patient, Pharma R&D)
- Incorporates a long-term perspective (All)
  - Often at least 1 year, possibly longer (Reg)
  - However, concerns that randomisation breaks down if patients move between treatments (Pharma)
  - Also concerns about delayed approval (Pharma, Pat)
- Opportunities for assessing compliance to treatment

* Stakeholder: Pharma R&D (Pharma), Health technology assessor (HTA), Patients (Pat), Regulatory (Reg)

Group 3

Stakeholders in this group included a patient representative and representatives from the pharmaceutical R&D, academics, physicians, and payers. The group indicted that PCTs would be useful for understanding real world acceptability of medicines and devices to patients but payers may only be interested if this translates into effects on outcomes. There was agreement that recruiting a broader patient population to provide an estimate of relative efficacy would be of value to all stakeholders, although there was divergence over how to analyse the data. Furthermore, PCTs could also capture earlier safety data in broader populations.

The group indicated these particular points on usefulness of PCTs:

- Population
  - There was agreement that including broader populations, (for example patients with co-morbidities and non-compliant patients) was useful but some stakeholders wanted to see the overall treatment effect in the total population whilst others (particularly patient representatives) wanted to understand the treatment effect in subgroups
  - Generalisability matters to everyone, patients, payers, industry
- Outcomes
  - For patients, endpoints about device use (ease of use and acceptability) and compliance are very important and it is not possible to fully address this in RCTs. However, payers needed to see the effect on outcomes
  - For collecting more representative health-related quality of life (HRQoL) and more patient functional (vs. biological) endpoints which cannot be addressed in conventional RCTs.
- PCTs could be useful when trying to demonstrate how a medicine could provide a paradigm shift in treatment strategy by comparing to real world treatment strategies
- Safety
  - To supplement or even replace Phase 4 studies
  - Earlier safety data in broader populations

Question 2: How strongly would results from pragmatic designs be accepted as evidence?

OBJECTIVE: Identify the factors that influence whether pragmatic trial data would be considered as "strong" or "weak" evidence and affect how it would be taken into account by decision makers.

Summary:

Strengths generally relate to **external validity** inherent in PCTs and weaknesses reflect lack of **internal validity** and difficulties with analyses (for example in subgroup analyses and dealing with treatment changes and multiple comparators).

It was stated that **clear objectives must be agreed** and prioritised by relevant stakeholders and included in a Reporting and Analysis Plan before study execution, to allow for studies to be **properly powered** for subgroup analyses.

For decision makers, evidence from PCTs would be **more acceptable for drugs with a known benefit/risk profil**e, and **less acceptable for drugs with a novel mechanism of action** because of uncertainties surrounding efficacy and safety profile of these drugs.

PCTs were seen as complementing RCTs; for instance they could be used to **justify clinical relevance** of new drugs to decision makers. PCTs should however not replace RCTs, because decision makers would still require **demonstration that treatment effects are consistent** with those observed in standard RCTs. As such, it was mentioned that a carefully formulated clinical development plan that plays on the strengths of RCTs and PCTs (i.e. the high internal validity of the former and the high external validity of the latter) would provide for the most efficient use of resources and timely drug delivery to patients. For example, the **inclusion of a broader patient population and more clinically relevant endpoints in a typical phase 3 RCT could be more timely and efficient than introducing a more real-world approach** with limited monitoring or other pragmatic elements in the development plan. Therefore, the development plan should address when it is beneficial, based on broad stakeholder perspectives, to incorporate a traditional RCT into development or when more elements of the pragmatic continuum (possibly gauged by PRECIS criteria) should be introduced.

Randomisation could break down following treatment switching and in long term studies and therefore the **robustness of long-term PCTs** was questioned.

Uncertainty regarding the most **appropriate trial design** and the most a**ppropriate evidence synthesis** could lead to difficulties in interpreting the results and therefore lessen acceptability by decision makers.

Group 1

The stakeholders noted that strengths and value of PCTs generally relate to external validity inherent in PCTs and weaknesses reflect lack of internal validity and difficulties with analyses (for instance subgroup analyses, dealing with treatment changes and additional comparators).

Rather than identifying the factors that influence whether PCT data could be considered strong or weak, the group focused on the specific circumstances when the PCTs would be of greatest benefit, and conversely when they would not be expected to be useful.

In which specific circumstances would PCTs be most beneficial?

- Before initial HTA assessment to provide an indication of clinical benefit in the general patient population (HTA)
- For drugs with a known benefit/risk profile – known molecules/5th in class – possible pre-launch (Pharma)

In which specific circumstances would PCTs not be beneficial?

- For new compound/new class – pre-launch very difficult (Pharma)

Group 2

PCTs were considered to be useful for understanding place in treatment paradigm and acceptability for patients and HTA. Oral insulin was mentioned as one example, where the drug was discontinued after launch because patients were finally not keen to use it. Perhaps a PCT at phase 3 would have identified this problem earlier.

Comments on the acceptability of PCTs:

- Interpretation of data arising from PCTs compared with RCT (HTA)
  - PCTs not blinded, potential lower effect, therefore uncertainty in overall effect estimates
- Added benefit; PCT supportive to justify clinical relevance but RCTs remain core (Reg)
- Place in treatment paradigm (Pat, HTA)
- Use of drugs, compliance (Pat)
  - inhaler technique for respiratory disease (HTA)
  - route of administration (Pharma)
- Outcomes (Pat)
  - Patients prefer outcomes that are clinical relevant. They should also be more objective; it is possible for patients to state they are fine all the time regardless of clinical reality
- Randomisation may break down in long term studies and therefore the robustness of long-term PCTs could be questioned by decision makers (Pharma, Reg)

* Stakeholder: Pharma R&D (Pharma), Health technology assessor (HTA), Patients (Pat), Regulatory (Reg)

Group 3

HTA stakeholders indicated that PCTs should be considered within the context of the development plan for a medicine. Both RCTs and PCTs would be taken into account, assuming randomisation and a comparative approach in the PCTs. If and RCT and PCT both examined the same objectives the group would expect consistency in direction and if size of effect differed, payers might want to understand why if that was not the case.

The group noted that PCTs could be affected by open label bias and this could lessen acceptability of data. Consideration of biases should be incorporated into the design at an early stage. Observer bias can be reduced through choice of endpoint.

Consensus was reached among all stakeholders in this group that clear objectives must be agreed and prioritised by relevant stakeholders and included in a Reporting and Analysis Plan before study execution allowing for the study to be properly powered for subgroup analyses.

It was noted that the choice of comparator is critical for decision-making and the payer may set the relevant comparator(s) for their healthcare system. Although indirect comparisons can be conducted, in some instances these may not meet the methods requirements of payers and thus additional PCTs or RCTs may need to be incorporated in the development programme to address this effectiveness challenge. If multiple comparators (for instance a physician choice standard of care arm) are included in a PCT it is necessary to ensure that analyses for the relevant comparator subgroup are powered as statistical significance on key endpoints is likely to be required by payers.

Breakout session 2

Following the presentations, participants joined their previous groups and discussed the third question:

Question 3: How can we maximise the value and acceptability of PCTs?

OBJECTIVE: How do we build on positive opportunities to utilise PCTs and address any barriers to acceptability? Generate solutions to mitigate concerns around using PCT data in decision making. For example: Scientific Standards and Best Practice; Scientific Advice and Review; Generalisability and Analysis Plans; Raising understanding of RWE and Patient-Centred Outcomes Research.

Summary:

Push from both regulators and HTA regarding whether the development programme answers the efficacy and effectiveness questions appropriately. There needs to be dialogue on how they fit into the evidence package as it may be unrealistic to ask for PCTs on top of requirements for RCTs.

Guidelines on trial designs, evidence synthesis and best practice should be developed, driven by input from academia, rather than pharmaceutical R&D. Initially they should be focused on overarching principles, rather than specific details. Multi-stakeholder case studies evaluating whether different degrees/elements of pragmatic design would be effective in reducing decision making uncertainty in different development scenarios were viewed as important to developing additional knowledge.

A **stepwise approach** was suggested in implementation of PCTs, starting by looking at RCTs and relaxing exclusion criteria and considering which aspects of the trial need to be more pragmatic.

Upskilling on methodology and evidence synthesis is needed in both pharma and public sectors. Simulations may be used to increase generalisability but will not be acceptable by all payers. Thus, there is a need for sufficient real-world data sources to inform simulations.

A framework is needed to **determine where efficacy/effectiveness gap is expected**. This determines where you need more pragmatism in trials.

Patients have a clear role in providing the "**authentic voice**" that is needed to make PCTs more accepted.

Exploration of **innovative trial designs**. For instance a hybrid PCT with an "RCT population" which could provide internal validity of the trial.

Document and characterise **options for limited PCT** that is only pragmatic to a certain extent. Pharma R&D and decision makers should co**nsider which pragmatic elements should be incorporated** in the PCT.

Group 1

Participants indicated that there needs to be requirement from both HTA and regulatory sides for PCTs to be included in evidence packages. Possible compromise needed on RCT requirements because seems unrealistic to ask PCT on top of total RCT package.

A stepwise approach was suggested in implementation of PCTs, starting by looking at RCTs and relaxing exclusion criteria and considering which aspects of the trial need to be more pragmatic. This was seen as a more acceptable option compared with implementation of pure PCTs in the short to medium term. One way of gauging how pragmatic an RCT is to ask sponsors to outline how pragmatic their RCT is, perhaps by using PRECIS or similar tools.

An implementation of early PCT may lessen requirement for post authorisation studies. This should be considered by pharma when assessing the value proposition of trials

Specific comments by stakeholder groups ("V" denotes comment on value and "A" on acceptance):

Pharma participants:

- A: Guidelines and good practice for PCTs needed
    - preferably HTA guidelines first, then companies will follow
    - pharma development is really risk-averse so need guidance from academia to move forward, this goes equally for HTA
- A: Champions needed in the public and private sectors who understand the role and value of PCTs. This highlights the need for upskilling
- A: Document and characterise options for limited PCT that only pragmatic to a certain extent. Pharma R&D and decision makers should consider which pragmatic elements should be incorporated in the PCT
- A: More space for PCT peri- and post launch or in conditional licencing
- V: need to have insight in the consequences of changing design options

HTA participants:

- V: PCTs for disease areas where PROs are more important, such as oncology
- V: PCTs for chronic diseases where you don't have hard endpoints

- A: HTA needs a mind shift towards the idea that RCT and PCT are not two opposites but are on continuum: analysing to what extent the designs they accept are already in some aspects pragmatic might help in this aspect
- A: To what extent can PCTs, if applied right, mitigate the need for post authorisation safety studies (PASS) or reduce their requirements?
- A: Possibility for PCT and RCT give different conclusions; need RCT to evaluate but combination of PCT & RCT is more appropriate
- If you claim that PCT are different from RCT do we need a gold standard?

Academia participants:

- Current trial system is too restrictive, need to move to pragmatic/simple, also pre-launch
- V: A lot of decisions in health care are currently not evidence-based, therefore there is a need for more trials in general
- There may be a role for more adaptive trials where the move is from closely monitored RCT to more PCT during the drug development process
- V: methodological guidelines are required
- V: need framework to determine where you expect difference between usual practice and RCT setting, because this determines where you need more pragmatism in your trial, for instance adherence, dosing in real practice. PRECIS is first step but not complete, need to make the link to whether you expect them to influence the outcome/drug effect

Group 2

The group formulated headline messages to pharmaceutical R&D who are considering PCTS:

The patient message: Bring patients into design discussions; ensure there is a clear benefit offered to patients and ensure all subsequent data are fully disclosed. This will facilitate buy-in from patients.

The regulator message: Ensure the resulting data will be reliable for regulatory purpose and consider the needs of HTAs. Understand what will make the study design and resulting data acceptable so that you don't get to the end before realising design could have been optimised

The HTA message: Ensure the PCT brings value beyond RCTs and focus on the rationale why a PCT might be required.

The group discussed a variety of ways in which acceptability of PCTs might be increased:

- A more standardised approach to design (Payer/HTA)
  - Potential to increase acceptability by HTA/payers if there was more standardisation of PRO, outcome measures and design features
  - Avoid over-emphasis on outcome bias. A reality, but can be managed; dependent on setting.
  - There are no menus available – no current best practice
- Create a dialogue to explore options (Payer/HTA/Pharma/Pat)
  - Use of joint scientific advice / multi-stakeholder discussions
  - "Safe harbour" discussions
  - Analyse – design study/run study and then analyse again, adjust design and so forth
- Increased generalisability of results

- For instance analytic techniques for modelling or extrapolating results
- Facilitating modelling of PCT results from one jurisdiction to another

- More education is required
  - Across all stakeholders
- PCTs would not be used on their own
  - Focus should be on situations where PCTs could complement traditional study designs
- Credibility would be increased if PCTs are used to show increased as well as decreased effectiveness compared to RCT efficacy
  - This will come with time, but can't be designed – no company develops a drug that they believe will have limited effectiveness in the RW
- Innovative hybrid/adaptive trial designs (Payer, Pharma)
  - PCT to include a RCT population. Could you run a pre-specified interim analysis which focuses on the RCT population using similar endpoints and run study for a similar period of time – this would help provide internally validity of the trial. The 'RW' trial would then continue on for a longer period with the broader patient population.
- Build on potential patient-related strengths (Pat)
  - Possible lower drop-out rates than RCTs if patients feel safe in clinical practice
  - Added value by patient feedback based on real world.

Group 3

The group indicated that while scientific standards and best practice need to be outlined, they should at this stage be concerned with overarching principles, rather than specific details, and learning should be built upon case studies.

- Scientific standards and best practice
  - Overarching principles would be helpful (not too much detail), particularly if from an international convention including payers
  - There was some scepticism on the value of standards so early in the development of this field of research and concern that scientific progress should not be restricted to a narrow approach.
  - Current advice was felt to be based on historical PCTs rather than looking at what it is possible to achieve
  - Best approach is to learn through real examples
  - Consider a standard set of endpoints for PCTs and for a disease (with patient input)
- Scientific advice and review
  - Critical to build experience in PCT design and review via case studies so that the field can advance through learning by example
  - Review of whole development programmes, rather than individual studies, will allow R&D to consider what activities can be stopped or reduced if additional PCTs are planned. It will also allow consideration of the most efficient ways of addressing effectiveness challenges within the programme, either by increasing pragmatism of typical RCTs or including new PCTs
- Joint agreement on core questions
  - Joint scientific advice should be sought to ensure that key stakeholders (regulatory, payer, patient, Pharma (both R&D and commercial)) agree on a limited number of core questions so that the PCT can be robustly designed to answer these (rather than diluting rigour by adding multiple additional objectives)

- Need for an "authentic patient voice"
  - Clear role for patients to input but consideration of the patient perspective should go beyond input into trial design and implementation. From early in development Pharma R&D should consider what patients want in a therapy area and how the development programme can address this.
  - Embrace the variability of the patient perspective (for instance needs, experience, disease etc.)
- Understanding of RWE and patient-centred outcomes
  - To increase the ability to publish PCT protocols and results
  - Increase publication reviewers' and clinicians' understanding
- Simulations and building up of experience
  - Increase observational data sources on the real world status quo and disease natural history in COPD (or relevant therapy area)
    - Collaboration of industry and academics
    - Include different healthcare systems and real world patient behaviour
    - These can then be used to simulate potential PCTs or generalise results from one locality to another

- Consider how to design all trials to best answer the pertinent questions i.e. consider increasing pragmatism (for instance by including broader population) in typical Phase 3 RCTs (it doesn't necessarily require a separate PCT)

- Generalisability
  - Some payers will not accept simulations to generalise results from a trial outside their healthcare setting (especially on healthcare system endpoints such as hospitalisations). The study must be conducted within the relevant healthcare system. Therefore, consider whether the effectiveness challenge can be answered by making multinational RCTs more pragmatic rather than conducting a single setting PCT.
- Revision of the evidence hierarchy to reflect the continuum of pragmatism within studies

"Patients' views"

A COPD patient emphasised that consistent input is required by patients throughout the development. The patient particularly encouraged trial designers and decision makers to involve patients as early as possible, especially on aspects related to drug delivery. The patient also highlighted aspects of conducting trials, which are sometimes overlooked, for instance how to communicate with patients and when to engage them.

The patient impressed on workshop participants that patients may have a range of emotions and feelings related to their condition and that required consideration of a more tailored approach, representing a spectrum of engagement. The patient encouraged all stakeholders to constantly consider the patients' need, in particular that patients want better drugs, and an option to participate and provide a meaningful input into the development of new drugs.